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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/528,320	10/11/2005	Pascal Dumy	1383-PCT-US-02	4534
35811 7590 06/27/2007 IP GROUP OF DLA PIPER US LLP ONE LIBERTY PLACE 1650 MARKET ST, SUITE 4900 PHILADELPHIA, PA 19103			EXAMINER KHANNA, HEMANT	
			ART UNIT 1654	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/528,320	Applicant(s) DUMY ET AL.	
	Examiner Hemant Khanna	Art Unit 1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 26 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 60-92 is/are pending in the application.
- 4a) Of the above claim(s) 63-65 and 67-92 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 60-62, 66 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This office action is in response to Applicant's remarks filed March 26, 2007. Applicant has cancelled claims 1-59 and reintroduced the subject matter of claims 36-59 in claims 69-92. Further, the applicant has amended claims 60 to introduce the language from the non-elected method of claim 36. Additionally, the applicant has traversed the Examiner's rejection under 35 USC 103.
2. **Claims 63-65** remain withdrawn from consideration as being drawn to non-elected species to which the search was not extended. In accordance with Markush practice, should Applicant's elected species not be found free of the prior art, the Examiner is not required to extend the search to other non-elected species.
3. **Method claims 67-68, and 69-92** that depend from or require the limitations of the product claim 60, remain withdrawn from consideration until the claim to the elected species is found allowable (see Examiner's Restriction under the Heading "Notice of Possible Rejoinder", pages 5 and 6, filed June 27, 2006).
4. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.
5. Claims 60-62, and 66 have been examined on the merits.

Claim Objections

6. (Withdrawn) Objection to claims 61-62 for minor informalities is withdrawn in view of Applicant's amendments to claims 61-62.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

8. (Maintained) Rejection of claims 60-62, 66 under 35 U.S.C. 103(a) as being unpatentable over Scheibler L. et al. (Angew. Chem. Int. Ed. (1999) Vol. 38, pages 696-699) in view of Kantlehner M. et al. (Angew. Chem. Int. Ed. (1999) Vol. 38, pages 560-562) and Rajopadhye M. et al (WO 99/58162) is maintained.

The claims are drawn to a grafted homodetic cyclopeptide, comprising peptide derived from cyclo(RGDfK) (SEQ ID NO:1) on one face and a detection agent on the other face.

Applicant's argue that the rejection based on the combined references cannot support a prima facie case of obviousness (Remarks, page 10). The Applicants argue that Scheibler teaches only one face of cyclopeptide that is available for

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functionalization. Applicants argue that Scheibler does not teach cyclopeptides whose one face was functionalized with a therapeutic/diagnostic.

Applicants argue that Kantlehner teaches the elected species that is anchored to an implant, thus only permitting one face of the cyclopeptide to be functionalized. Applicant's argue that Kantlehner does not teach grafting the cyclopeptide on both sides because doing so would destroy the intended purpose of the cyclopeptides.

Applicants argue that Rajopadhye does not teach that the non-peptide linker would substitute the homodetic cyclopeptide. Hence, based on the above, the Applicants conclude that the combination of references do not teach any motivation to combine.

Applicant's further argue based on their citation of Peri, which discloses oxime bonds but teaches away from bioconjugates, to conclude that there was no reasonable expectation of success to combine the teachings in the references cited by the Examiner.

The Applicant's further argue that none of the references teach the functional limitations of "cell targeting" and therapeutic/diagnostic functions".

Finally, Applicant's argue the unobviousness of the instant grafted homodetic cyclopeptide based on product-by-process, suggesting that the homodetic cyclopeptide of Scheibler was prepared by the cyclization of a lysine residue, which resulted in epimerization of lysine during the preparation. As the instant preparation utilizes cyclization of a glycine residue, the Applicant's argue that the instant cyclization is evidence of an unexpected result.

Applicant's arguments have been considered but are not found persuasive.

The Applicant is reminded that instant claim 60 as originally filed, and after amendment is drawn to a product-by-process claim. Applicant is respectfully reminded that any functional limitations, such as "cell targeting" and therapeutic/diagnostic functions" are considered to determine if they materially change the product. In the instant case, there is insufficient information to determine that the functional limitations limit the product with a specified structure as given by the SEQ ID NO: 1 or a therapeutic or diagnostic with unspecified structure. The Applicant has argued that the Scheibler reference teaches the preparation of a homodetic cyclopeptide from lysine, while the instant claims are drawn to a product obtained by the cyclization of glycine, the Examiner respectfully submits that the determination of patentability of a product-by-process claim is based on the product, and hence the Applicant's arguments that the preparation of such peptides from the cyclization of glycine makes the instant invention unobvious is moot. See MPEP 2113.

Whether Scheibler's process resulted in the epimerization of lysine is moot, in view of Applicants own submission (Remarks, paragraph 6, page 14) that the desired cyclopeptide was still produced alongside the undesired side product, thus rendering the product in the instant claims as obvious.

Further, the Examiner does not agree that with the Applicant's argument that Kantlehner does not teach grafting the cyclopeptide on both sides because doing so

would destroy the intended purpose of the cyclopeptides. There is nothing in the Kantlehner reference that teaches away from the intended purpose of the recognition derived from grafted cyclopeptides.

The Examiner does not agree with Applicant's arguments based on their citation of Peri, which discloses oxime bonds but teaches away from bioconjugates, to conclude that there was no reasonable expectation of success to combine the teachings in the references cited by the Examiner. Nothing in the Scheibler reference, which teaches the conjugation of antigenic peptides to the homodetic RAFT via oxime bonds (left column, paragraph 1, page 697), suggests that the preparation of bioconjugates was unsuccessful.

The Examiner further submits that the Applicant's arguing against references individually wherein the rejection is based on the combination of references does not make the instant invention nonobvious. See MPEP 2145 (IV).

The Examiner respectfully submits that the content of the prior art as exemplified by persons having ordinary skill (Scheibler, Kantlehner, and Rajopadhye) at the time of the invention, provides the motivation to combine references. One of ordinary skill would have the capability of understanding that homodetic cyclopeptides as disclosed by Scheibler can be extended in conjunction with methodologies available (Kantlehner, and Rajopadhye) to the construction of multifunctional cyclopeptides with grafted upper and lower face (Scheibler, right column, last paragraph, page 698), and would immediately see that the thing to do would be to solve the problem of delivery and

localization of pharmaceuticals in the angiogenic tumor vasculature via functionalizing one carrier (Rajopadhye and Scheibler) as argued in the previous office action.

The US Federal Circuit has recently explicitly stated that in order to make a prima facie case of obviousness, the suggestion and motivation to combine said references need not be explicitly stated in the text of the references. Rather, consideration of common knowledge and common sense when combining references is not only permitted but required. See *DyStar Textilfarben GmbH & Co. Deutschland KG v. C.H. Patrick Co.*, 80 USPQ2d 1641 (Fed. Cir. 2006).

MPEP 2143.01 (I) states "There are three possible sources of motivation to combine references: the nature of the problem to be solved, the teachings of the prior art, and the knowledge of persons of ordinary skill in the art". "The test for an implicit showing is what the combined teachings, knowledge of one of ordinary skill in the art, and the nature of the problem to be solved as a whole would have suggested to those of ordinary skill in the art".

The motivation to combine the references arose from the nature of the problem to be solved taken as a whole (Rajopadhye and Scheibler). The instant claimed invention is unpatentable if the differences between it and the prior art are not sufficiently great that the subject matter as a whole would have been obvious at the time the invention was made by one of ordinary skill in the art.

The Examiner argues that the use of Scheibler, Kantlehner and Rajopadhye taken together would have the advantage of grafting a homodetic cyclopeptide on both faces. Hence, the Examiner respectfully submits that it would be prima facie obvious to

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one of ordinary skill in the art to take the combination of old features to prepare a homodetic cyclopeptide grafted on two faces with a moiety of SEQ ID NO:1 that targets the integrin receptor and a radiopharmaceutical.

Rejection is maintained.

Conclusion

9. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Hemant Khanna Ph. D.
June 15, 2007



DAVID LUKTON, PH.D.
PRIMARY EXAMINER